Susceptibility-Weighted Imaging in Carotido-Cavernous Fistulas

A Case Control Study

KAMBLE JAYAPRAKASH HARSHA, RAM SHENOY BASTI,
CHANDRASEKHARAN KESAVADAS, BEJOY THOMAS

Department of Imaging Sciences and Interventional Radiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology; Thiruvananthapuram, India

Key words: carotico-cavernous fistula, susceptibility-weighted imaging, magnetic resonance imaging

Summary

This study determined the utility and accuracy of susceptibility-weighted MRI (SWI) for the detection of carotid cavernous fistulas.

We retrospectively compared SWI images in nine patients (Group 1, case group) of DSA-proved carotid cavernous fistula (CCF) and 19 DSA negative cases for CCF as a control group (Group 2). Group 1 was again sub-grouped into direct and indirect types. Using uniform region-of-interest measurements, signal intensity within the superior ophthalmic vein (SOV) and the superior sagittal sinus (SSS) were measured on magnitude images of SWI. The SOV/SSS signal intensity ratio was calculated in each case and the mean values of the two groups were compared.

Eleven SOV/SSS signal intensity ratios in Group 1 (7 unilateral and two bilateral CCF), 38 in Group 2 (both sides in 19 control subjects) were included. Median $\pm$ interquartile range of SOV/SSS ratios for Group 1, Group 2, indirect and direct type CCFs were 1.07 ± 0.43 , 0.39 ± 0.23 , 0.83 ± 0.29 , 1.4 ± 0.38 respectively. Mann-Whitney test between Groups 1 and 2 was statistically significant with $P < 0.0001$. All cases and controls were reliably distinguished with SOV/SSS signal intensity ratio of 0.64 as cut-off. Direct CCF cases had consistently higher ratios than indirect CCF. SWI was highly sensitive for detection and differentiation of both direct and indirect CCF. Only one case of corticovenous reflux was missed by SWI.

SWI is useful for detection of CCF and to differentiate between direct and indirect CCF.

Introduction

Susceptibility-weighted imaging (SWI) is a relatively new MR imaging sequence, with rapidly evolving applications. The technique utilizes both phase and magnitude images from a high resolution, three-dimensional fully velocity-compensated gradient echo sequence¹. Detecting susceptibility effects aids in the identification of cerebral microbleeds, hematomas, calcification and mineralization in the brain. The ability of SWI to detect arterialized flow as hyperintensity is based on the lack of T2* effect of oxyhaemoglobin and inherent exquisite sensitivity of this sequence to time-of-flight effect, while the hypointensity of veins is due to blood oxygen level-dependent (BOLD) contrast². However, in cases of arterialized veins secondary to arteriovenous shunting, veins also exhibit hyperintensity¹⁻³.

Recently a few authors reported the usefulness of SWI in cerebral arteriovenous shunting. George et al. studied the utility of SWI in cerebral AVM, and described feeding artery, AVM nidus and draining vein appearances on SWI sequence⁴. Noguchi et al. described SWI utility in dural arteriovenous fistula detection^{5,6}. The usefulness of the SWI sequence in brain and spine fistulas were also described by Fujima et al., Saini et al. and Tsui et al.⁷⁻⁹. A larger series studied by Jagadeesan et al. described the utility of SWI magnitude image in brain arteriovenous malformations¹⁰. However, the utility of SWI in CCF has not been previously studied to the best of our knowledge.

This study attempted to determine the utility and accuracy of susceptibility-weighted MRI (SWI) for the non-invasive detection of carotid cavernous fistulas (CCFs) and to distinguish between direct and indirect CCFs. We hypothesized that abnormal hyperintensity signal of superior ophthalmic veins/inferior petrosal sinus on SWI images was secondary to arterialized blood flow from CCF. In addition, we aimed to identify a control group to compare the statistical significance of our findings in the case group.

Materials and Methods

Patient Selection

The study was approved by the Institutional Review Board. Informed consent for all studies had been obtained both for magnetic resonance imaging (MRI) and digital subtraction angiography (DSA) separately prior to the procedure. We retrospectively evaluated all consecutive CCF patients from the institute's Picture Archiving and Communications systems between January 2009 and October 2011. Exclusion criteria were: 1) either or both SWI and DSA not available for comparison; 2) artifact in the study which prevented proper interpretation; 3) interval between the two studies were more than three months. Dural arteriovenous fistula, arteriovenous malformation or aneurysm cases were also excluded from the control group which might affect SOV size/signal intensity. There were 38 cases of CCF, of which 20 had both DSA and SWI. Nine cases were excluded as the interval between the two studies was more than three months and two had motion artefacts significantly affecting image quality. Finally nine cases were included in Group 1. In the control group (Group 2), 19 age and sex-matched controls without CCF, who had undergone cerebral DSA for other indications, also having SWI images for comparison were included. Group 1 was further subdivided into direct and indirect CCF groups (three direct and six indirect).

Medical Records Review

Medical records were reviewed for patient demographic details like age, sex, clinical presentation, time interval between DSA and MRI study, treatment given including medical and endovascular therapy and follow-up.

Image Acquisition

MR Imaging of the brain was done using a 12-channel matrix coil on a 1.5T clinical scanner (Avanto, SQ Engine; Siemens, Erlangen, Germany). The following sequences were obtained: axial T1-, T2-, proton density (PD), SWI, and post contrast T1-weighted images. The SWI sequence parameters were as follows: TR (repetition time), 48 ms; TE (echo time), 40 ms; Flip angle, 20°; bandwidth, 80 kHz; slice thickness, 2 mm, with 56 slices in a single slab; matrix size, 512×256, iPAT factor-2. The acquisition time was 2.58 minutes. A fully flow-compensated sequence was used. In each case, four image series were available: SWI, phase, magnitude, and minimal intensity projection (min-IP). Contrast study was done after acquisition of SWI in all cases.

DSA was performed using a biplane neuroangiographic suite (Innova 3131, GE Medical Systems, LLC, Milwaukee, WI, USA). After obtaining transfemoral arterial access and achieving systemic anticoagulation by heparin, a diagnostic catheter (size 4F or 5F) was carefully navigated into bilateral external and internal carotid arteries, unilateral or bilateral vertebral arteries. The catheter tip was positioned in the selected cerebral vessel, angiographic images in standard angiographic projections were acquired by injecting iodinated contrast. Adequate haemostasis was achieved after removal of the sheath.

Image Analysis

In both case and control groups, utilizing conventional non-contrast and contrast-enhanced MRI and MRA, the superior ophthalmic vein (SOV) on either side was identified. A five pixel region-of-interest (ROI) was placed at the corresponding site in magnitude images of SWI sequence to measure the signal intensity (Figure 1). However in one patient with no SOV drainage but inferior petrosal drainage, the ROI was kept in the inferior petrosal sinus. Another five pixel ROI was placed in the posterior third of the superior sagittal sinus (SSS) and this was taken as the internal reference standard against which SOV intensity was compared. In both groups, SOV/SSS signal intensity ratio was calculated on either side separately. In one patient without SOV drainage, the inferior petrosal sinus was measured instead of SOV.

↑ Figure 2 Box and whiskers plot for three data groups, direct and indirect CCF shown separately, followed by control group. All three groups are statistically significant ($P < 0.05$). The mean values for each group are annotated (1.34, 0.84 and 0.40). The boxes span the range of SOV signal intensities from the 25th to 75th percentiles. The bars within the boxes denote the median value, whereas the vertical lines ("whiskers") are reflective of the data range.

← Figure 1 Shows the placement of region-of-interest (ROI) on the superior ophthalmic vein and in the superior sagittal sinus on magnitude images of SWI sequence to measure the signal intensity ratio.

Statistical Analysis

Statistical analysis was performed using SPSS 17.0 software. Statistical significance for the signal intensity ratio of superior ophthalmic vein was determined: superior sagittal sinus on SWI compared to DSA between Group 1 and Group 2 using Mann-Whitney test. In addition, statistical significance was determined between direct and indirect CCFs.

Results

Group 1 consisted of nine patients, two men and seven women (mean age 47.1, range 32-60 years), while Group 2 consisted of 19 patients, five men and 14 women (mean age of 43.6, range 30-58 years) (Table 1). The control group included seven cases of vasculitis, four strokes, one epilepsy, one cavernoma, one aspergilloma, two asymmetric cavernous sinuses, one pachymeningitis, one occipital meningioma and a demyelination. There were 11 SOV (three direct and six indirect CCFs) in Group 1, 38 SOV

in Group 2 for analysis. Group 1 was further subdivided into three direct SOV and eight indirect SOV and a separate subgroup analysis was done.

Mean $\pm$ Standard deviation of SOV/SSS signal intensity ratios for Group 1, Group 2, indirect and direct types were 1.07 ± 0.43 , 0.39 ± 0.23 , 0.83 ± 0.29 , 1.4 ± 0.38 respectively. The results are summarized in the box plot (Figure 2). Mann-Whitney (two-tailed) test between Groups 1 and 2 for detecting CCF was statistically significant with $P < 0.0001$. Accuracy was determined, taking DSA as standard reference; SWI was 100% sensitive and specific for detection of CCF. All cases and controls were distinguished with an SOV/SSS signal intensity ratio of 0.64 as cut-off with 100% sensitivity and specificity. Direct CCF cases consistently had higher ratios than indirect CCF. With an SOV/SSS signal intensity ratio value of 1 as cut-off, direct and indirect CCFs were distinguished with 100% sensitivity and specificity (Figure 2). However one case of corticovenous reflux detected in DSA was missed in conventional MR imaging and in the SWI sequence.

Figure 3 A) Axial TOF MRA source image show signal loss due to saturation effect in SOV. B) Corresponding axial magnitude image show hyperintensity in SOV.

Discussion

Carotico-cavernous fistula is an abnormal communication between the internal or external carotid artery and the cavernous sinus. High flow fistulas (Barrow type A) are usually post traumatic and are relatively easy to diagnose and identify due to their typical clinical presentation. However low flow spontaneous fistulas (Barrow types B, C, D) are of indirect type, develop typically in middle-aged women, with subtle clinical symptoms and signs³. Other entities like thyroid ophthalmopathy and orbital pseudotumour can have a similar clinical picture. In the case of rapid progression of symptoms, cavernous sinus and superior ophthalmic vein thrombosis also need to be considered. These patients are at 30% risk of developing visual loss due to increased intraocular pressure, *ischemic optic neuropathy*, retinal vessel occlusion, and/or even proliferative retinopathy followed by tractional retinal detachment¹¹.

Arterialized blood flow in SOV remains the mainstay for diagnosis of CCF by imaging. Transcranial Doppler can detect high flow fistulas

well¹². CT, CTA, conventional MRI, TOF MRA, and CEMRA are utilized for CCF detection^{13,14}. Chen et al. compared CCF detection by CTA, MRA against gold standard investigation DSA, showed CTA source images to be superior to MRA, though the sensitivity remained low (76%)¹⁵. No other large studies are available comparing the sensitivity and specificity of these investigating modalities in detection of CCF.

MRI is the initial modality of investigation in many cases. But MRI/MRA has many limitations: 1) Asymmetric hyperintensity of the cavernous sinus may be the only finding in the MRA source image, which may be missed¹⁶; 2) Minimal prominence or asymmetry of the cavernous sinus may be mistaken for other pathologies like pseudotumour; 3) Tanka et al. described high signal intensity in cavernous sinus on MRA in 4%–36% of asymptomatic patients¹⁷. The probable mechanism behind this finding was incompletely saturated venous blood entering the cavernous sinus from the superficial middle cerebral vein or the superior petrosal sinus; 4) Frequent identification of normal cav-

Table 1 Summary of case group characteristics

CASE GROUP							
Case No	Age/sex	CCF type			SOV SI	SSS SI	SOV/SSS SI ratio
1	60yr/F	Indirect	Bilateral	R	307	430	0.71
				L	359		0.83
2	34yr/M	Direct	Left side	L	434	387	1.12
3	50yr/F	Indirect	Bilateral	R	317	315	1.00
				L	299		0.94
4	58yr/F	Direct	Right side	R	461	329	1.40
5	42yr/F	Direct	Right side	R	548	365	1.50
6	32yr/F	Indirect	Left side	L	298	465	0.64
7	49yr/F	Indirect	Left side	L	250	300	0.83
8	43yr/M	Indirect	Left side	L	330	460	0.71
9	56yr/F	Indirect	Left side	L	164	257	0.64

CCF: carotid cavernous fistula; SOV: superior ophthalmic vein; SSS: superior sagittal sinus; SI: signal intensity; CNS: central nervous system.

ernous sinus or inferior petrosal sinus signal on 3D TOF MR angiogram is dependent on technical factors that vary among scanners, adding to the confusion between CCF and other differentials¹⁸; 5) Contrast administration always has added risk to patient (0.7%-2.4%)¹⁹. The time-resolved MRA technique is a promising non-invasive technique with high sensitivity and specificity in detecting corticovenous reflux, but it still requires contrast administration²⁰.

DSA remains the gold standard for diagnosis of CCF, but is invasive and cannot be performed at each follow-up. Patients are often subjected to multiple investigations like ocular Doppler, MRI and CTA prior to DSA. The differential diagnoses for CCF are diverse compared to brain AVM and dural arteriovenous fistulas. Accurate diagnosis of CCF by a non-invasive modality is important. Apart from diagnosis of CCF, accurate differentiation between high flow and low flow fistula is also important for management decisions.

Our results suggest the usefulness of SWI in all (100%) studied cases to diagnose CCF and differentiate between low and high-flow fistulas. SOV/SSS signal intensity ratio corresponded to the grade of shunting. As DSA is required for confirmation of low-flow fistulas, in SWI-identified CCF cases, additional investigations like CEMRA and CTA can be avoided. Many indirect CCF are being misdiagnosed as chronic conjunctivitis and may remain undetected for years so that the SWI sequence can be problem-solving tool in such instances.

In CCF patients with dilated SOV, TOF MRA may show low signal intensity due to the saturation effect of slow flow and inclination of SOV parallel to TOF saturation band (Figure 3) while SWI shows high signal intensity indicating the superiority of SWI over TOF MRA. Even in patients with no orbital signs or prominent cavernous sinus and minimal SOV prominence (Figure 4), SOV/SSS signal intensity ratio was high, confirming the usefulness of this sequence.

In CCF patients without dilated SOV and the fistula drained by the inferior petrosal sinus (IPS) alone, SWI identified high signal intensity in IPS. This finding may be helpful in spontaneous superior ophthalmic vein thrombosis or partially treated CCF cases to identify the residual fistula. Doppler or other imaging modality cannot identify IPS drainage reliably leading to a false diagnosis of complete cure.

SWI may also be useful in the follow-up of treated CCF patients for possible recurrence, residual disease or cure. Twenty to forty-five percent of patients with low-flow fistulas may be cured spontaneously or with manual carotid compression and such patients can reliably be screened by the SWI sequence.

Our study has limitations like the small number of cases studied. Though SWI appears to be helpful in the early diagnosis and follow-up of CCF, this needs to be evaluated by larger prospective studies. Second, the presence of other dural arteriovenous fistulas in the same patient may alter the signal intensity of SSS, which may increase false negative cases. Paksoy

Figure 4 A 50 year-old female, presented with diplopia under evaluation. A) Axial T2-weighted image shows no proptosis. However SOVs were prominent (arrow). B, C) Magnitude image in axial and reformatted coronal image demonstrating high signal intensity SOV (arrows). D) Arterial phase of left carotid angiogram in lateral projection demonstrating indirect carotid cavernous fistula.

et al. reported high signal intensity in the inferior petrosal sinus from retrograde flow due to blood stealing from the internal jugular vein toward the cavernous sinus secondary to central venous stenosis. Such phenomenon may contribute to false positivity by SWI²¹. Third, superficial cortical venous reflux was noted in DSA in one case of direct CCF, but corresponding hyperintensity was not seen in SWI, which is important for CCF prognostication. The presence of corticovenous reflux at initial diagnosis

mandates immediate treatment. In addition, the inability of SWI to detect corticovenous reflux development during follow-up constitutes a major limitation of this technique. This may be secondary to the low sensitivity (50%) of SWI in the detection of cortical venous reflux, though further study in CCF would answer the question correctly. Fourth, SWI is highly susceptible to local field inhomogeneities, so its role in partially or completely treated CCFs may be limited (i.e. presence of coils).

Conclusion

Detection of SWI hyperintensity in the superior ophthalmic vein appears to be a reliable indicator of the presence of carotico-

cavernous fistula. SWI may also be useful to differentiate between direct and indirect CCF.

Its inability to detect corticovenous reflux is a major limitation of the SWI technique.

References

- 1 Barnes SR, Haacke EM. Susceptibility-weighted imaging: clinical angiographic applications. *Magn Reson Imaging Clin N Am*. 2009; 17: 47-61.
- 2 Haacke EM, Mittal S, Wu Z, et al. Susceptibility-weighted imaging: technical aspects and clinical applications, part 1. *Am J Neuroradiol*. 2009; 30 (1): 19-30.
- 3 Barrow DL, Spector RH, Braun IF, et al. Classification and treatment of spontaneous carotid-cavernous fistulas. *J Neurosurg*. 62: 248-256.
- 4 George U, Jolappara M, Kesavadas C, et al. Susceptibility-weighted imaging in the evaluation of brain arteriovenous malformations. *Neurol India*. 2010; 58 (4): 608-614.
- 5 Noguchi K, Kuwayama N, Kubo M, et al. Intracranial dural arteriovenous fistula with retrograde cortical venous drainage: use of susceptibility-weighted imaging in combination with dynamic susceptibility contrast imaging. *Am J Neuroradiol*. 2010; 31 (10): 1903-1910.
- 6 Letourneau-Guillon L, Krings T. Simultaneous arteriovenous shunting and venous congestion identification in dural arteriovenous fistulas using susceptibility-weighted imaging: initial experience. *Am J Neuroradiol*. 2012; 33 (2): 301-307.
- 7 Fujima N, Kudo K, Terae S, et al. Spinal arteriovenous malformation: evaluation of change in venous oxygenation with susceptibility-weighted MR imaging after treatment. *Radiology*. 2010; 254 (3): 891-899.
- 8 Saini J, Thomas B, Bodhey NK, et al. Susceptibility-weighted imaging in cranial dural arteriovenous fistulas. *Am J Neuroradiol*. 2009; 30 (1): E6.
- 9 Tsui YK, Tsai FY, Hasso AN, et al. Susceptibility-weighted imaging for differential diagnosis of cerebral vascular pathology: a pictorial review. *J Neurol Sci*. 2009; 287 (1-2): 7-16.
- 10 Jagadeesan BD, Delgado Almandoz JE, Moran CJ, et al. Accuracy of susceptibility-weighted imaging for the detection of arteriovenous shunting in vascular malformations of the brain. *Stroke*. 2011; 42 (1): 87-92.
- 11 Miller NR. Diagnosis and management of dural carotid-cavernous sinus fistulas. *Neurosurg Focus*. 2007; 23 (5): E13.
- 12 Flaharty PM, Lieb WE, Sergott RC, et al. Color Doppler imaging. A new noninvasive technique to diagnose and monitor carotid cavernous sinus fistulas. *Arch Ophthalmol*. 1991; 109 (4): 522-526.
- 13 Anderson K, Collie DA, Capewell A. CT angiographic appearances of carotico-cavernous fistula. *Clin Radiol*. 2001; 56 (6): 514-516.
- 14 Ikawa F, Uozumi T, Kiya K, et al. Diagnosis of carotid-cavernous fistulas with magnetic resonance angiography-demonstrating the draining veins utilizing 3-D time-of-flight and 3-D phase-contrast techniques. *Neurosurg Rev*. 1996; 19 (1): 7-12.
- 15 Chen CC, Chang PC, Shy CG, et al. CT angiography and MR angiography in the evaluation of carotid cavernous sinus fistula prior to embolization: a comparison of techniques. *Am J Neuroradiol*. 2005; 26 (9): 2349-2356.
- 16 Rucker JC, Biousse V, Newman NJ. Magnetic resonance angiography source images in carotid cavernous fistulas. *Br J Ophthalmol*. 2004; 88: 311.
- 17 Tanka H, Fujita N, Hirabuki N, et al. Origin of high signal intensity in the cavernous sinus in MR angiographic source images: correlation between MR and conventional angiography. *J Comput Assist Tomogr*. 2004; 28: 728-734.
- 18 Ouanounou S, Tomsick TA, Heitsman C, et al. Cavernous sinus and inferior petrosal sinus flow signal on three-dimensional time-of-flight MR angiography. *Am J Neuroradiol*. 1999; 20 (8): 1476-1481.
- 19 American College of Radiology. Manual on Contrast Media. Available at: <http://www.acr.org/~media/ACR/Documents/PDF/QualitySafety/Resources/Contrast%20Manual/FullManual.pdf>.
- 20 Meckel S, Maier M, Ruiz DS, et al. MR angiography of dural arteriovenous fistulas: diagnosis and follow-up after treatment using a time-resolved 3D contrast-enhanced technique. *Am J Neuroradiol*. 2007; 28 (5): 877-884.
- 21 Paksoy Y, Genç BO, Genç E. Retrograde flow in the left inferior petrosal sinus and blood steal of the cavernous sinus associated with central vein stenosis: MR angiographic findings. *Am J Neuroradiol*. 2003; 24 (7): 1364-1368.

Dr Thomas Bejoy, MBBS, MD
Department of Imaging Sciences
and Interventional Radiology
Sree Chitra Tirunal Institute
for Medical Sciences and Technology
Medical College P.O.
Thiruvananthapuram, 695001 India
E-mail: drbejoy2002@yahoo.com